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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,375	05/10/2005	Yuman Fong	08582/014002	5371

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EXAMINER	
HAMA, JOANNE	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/505,375	FONG ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-13 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/25/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of January 11, 2008 on May 9, 2008. Claims 2, 14-27 are cancelled. Claims 1, 28 are amended.

Claims 1, 3-13, 28 are under consideration

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) on January 25, 2008. The IDS has been considered.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-6, 8-13, 28 remain rejected in modified form under 35 U.S.C. 102(e) as being anticipated by Fong et al., US 2002/0071832 for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, July 14, 2007, and January 11, 2008.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant has amended claim 1 such that the subject has metastasis present at a site distal to the site of surgical resection of the tumor in the subject. Similarly, claim 28 has been amended such that the subject has regional lymphatic metastases present at a site distal to a site of surgical resection of a tumor in the subject. With regard to these limitations that the metastases are distal to the site of resection, Fong et al. envisioned that the promoters that are used to drive expression of a therapeutic agent (such as those listed in Fong et al., page 4, parag. 29) include the mts1 promoter, which is specific for metastatic tumors (Fong et al., page 5, parag. 34). A copy of Tulchinsky et al., 1992, PNAS, USA, 89: 9146-9150, which Fong et al. referred to as being a metastatic-specific promoter, is provided to Applicant. As such, Fong et al. envisioned that the claimed method can be used in patients with metastatic cancer and thus anticipate the instant claims.

Applicant's arguments filed May 9, 2008 have been fully considered but they are not persuasive.

Applicant indicates that Fong does not mention the treatment of metastases at a site distal to the site of surgical resection of a tumor, and thus, Fong does not expressly anticipate the present claims. Applicant indicates that inherent anticipation does not apply. Applicant indicates that applying these principles to the present case, Fong does

not inherently teach the present invention as the methods of Fong would not necessarily result in the treatment of the metastases that are the focus of the present claims, as not all tumors treated according to Fong would have produced metastases. Thus, treatment of metastases at a site distal from the site of surgical resection does not "necessarily flow" from the method of Fong (Applicant's emphasis, Applicant's response, pages 3-4). In response, this is not persuasive. As discussed above, Fong et al. envisioned that the method of resecting a tumor and administering an oncolytic herpes virus could be used in the situation where a patient has metastases. This is illustrated by the fact that Fong et al. teach that a metastatic cancer-specific promoter could be used in the claimed invention (Fong et al., page 5, parag. 34). As such, Fong et al. anticipate the instant claims.

Applicant indicates that Fong teaches a genus of treating cancer, in general, but Fong does not teach the species of treating metastases, as is now claimed. Applicant refers to MPEP 2131.02, wherein the prior art teaching of genus many only anticipate a species if the species can at once be envisaged from the genus. In response, this is not persuasive. First, an artisan would determine that Fong et al.'s teaching is applicable to metastatic cancer, as an artisan would recognize that the parenteral routes of administration (e.g. intravenous, see Fong et al., page 5, parag. 36) are used to treat metastatic cancer. This is supported by the art teaching that intravenous administration is desirable for treatment of metastatic disease or non-discrete tumors (Henderson et al., US Patent 6,406,861 B1, patented June 18, 2002, col., 3 lines 8-9). In addition to this issue, Fong et al. teach that the instant method was intended to treat metastatic

cancer as Fong et al. teach that a metastatic tumor-specific promoter, mts1, is envisioned to be used in their method (Fong et al., page 5, parag. 34). As such, Fong et al. envisioned the method to be applicable to metastatic cancer.

With regard to claims 3, 4, 28, wherein lymphatic metastasis is treated, Applicant indicates that Fong does not teach the treatment of any metastases, let alone lymphatic metastases. Fong does not inherently anticipate this claim, as carrying out the method of Fong does not necessarily result in the treatment of such metastases, as not all cancers treated using the method of Fong would have them. In response, as discussed above, Fong et al. envisioned that the method of administering oncolytic herpes virus to resected tumors would treat metastatic cancers as Fong et al. teach that a metastatic cancer-specific promoter could be used in their method. As such, while Fong et al. do not specifically indicate that their method could treat lymphatic metastases, their method would inherently do so.

Thus, the claims remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al., US 2002/0071832 in view of Wong et al., 2001, Human Gene Therapy,

12: 253-265, for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, July 24, 2007, January 11, 2008.

Applicant's arguments filed May 9, 2008 have been fully considered but they are not persuasive.

Applicant indicates that Fong does not anticipate the instant claims as Fong does not expressly teach the treatment of metastases, and inherency also cannot be found, as carrying out the method of Fong does not necessarily result in the effects of the method of the present claims (see response to 102 rejection). As such, Applicant submits that the teachings of Fong should be considered only with respect to killing of cancer cells at the site of surgical resection and virus administration. There is no mention in either Fong or Wong of the treatment of metastases that are present at a site distal to the site of surgical resection. Further, Applicant indicates that it was not known prior to the present invention that virus administered to a surgical bed could travel from the site of the surgical bed by any means (including via the lymphatic system). As this concept was not known, Fong does not provide any suggestion or motivation to carry out the presently claimed invention (Applicant's response, pages 6-7). In response, this is not persuasive. As discussed above, Fong et al. envisioned that the method of resecting a tumor and administering oncolytic herpes virus could be used to treat metastatic cancer. Guidance was provided by the fact that Fong et al. teach that the oncolytic virus be administered intravenously (which Henderson et al. teach is desirable for treatment of metastatic cancer) and that Fong et al. contemplate that a metastatic cancer-specific promoter can be used in their method. As such, Fong et al. provide

guidance to practice the claimed invention. With regard to Wong et al., Wong was provided to show that NV1023 was known at the time of filing and it was used in cancer therapy as an oncolytic virus. Because G207 and NV1023 were known at the time of filing to be oncolytic viruses, an artisan would have substituted one for the other to arrive at the claimed method.

Thus, the claims remain rejected.

Claims 1, 3-6, 8, 9, 28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al., 1999, FASEB J. 13: 1325-1334, in view of Rodgers and McCall, 2000, British Journal of Surgery, 87: 1142-1155, for reasons of record, February 12, 2007, July 24, 2007, January 11, 2008.

Applicant's arguments filed May 9, 2008 have been fully considered but they are not persuasive.

Applicant indicates that in a prior reply, the focus of Kooby was to reduce local recurrences and that there was no suggestion or motivation to treat metastases, such as lymphatic metastases. Applicant also indicates that the obviousness rejection is based on the concept of inherency. Applicant refer to the discussion regarding inherency and that in order for inherency to apply, an "allegedly inherent characteristic must necessarily flow from the teachings of the applied art" and that "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic" (MPEP 2112). In carrying out the approach of Kooby, the method of the instant invention requiring the treatment of

metastases may not take place in some instances, when there are no metastases to treat. Thus, as a required feature of the present invention (treatment of metastases) is not necessarily present in the method of Kooby, the principles of inherency do not apply (Applicant's response, page 8). In response, Kooby et al. teach a method of treating metastases (Kooby et al., page 1327, 1st col., under "Treatment of hepatic metastases with regional vascular infusion of G207") and as such, Kooby et al. remains obvious to the instant invention. While Applicant indicates that Kooby et al. teach reduction of local recurrences, it is noted that Kooby et al. teach metastatic cancer and that the recurrences are not necessarily local. While Kooby et al. teach that their study focuses on tumor development in liver, this is not indicative that the metastatic cancer cells used in their study do not form tumors in other parts of the body, such as the lymph nodes or lung. As an example of being metastatic and developing in other tissues, Kooby et al. teach that metastatic tumor cells were injected into spleens of rats and that 60 to 100 countable liver metastases were seen within 3 weeks of tumor challenge (Kooby et al., page 1327, 1st col., under "Treatment of hepatic metastases with regional vascular infusion of G207"). As such, Kooby et al. teach that cancer cells seeded in one area of the body can metastasize and develop in other regions of the body, including liver. Because Kooby et al. teach a method of treating metastases in liver with G207 and teach that metastatic cancer patients who have tumors in their livers often have their tumors resected (Kooby et al., page 1325, 2nd col., 1st parag.), it would have been obvious for an artisan to combine both cancer treatment methods. With regard to administration of virus to the resected site, an artisan would have done so to lyse the

cancer cells which may have been missed during the surgery. While the art does not specifically indicate that virus administered to the resected site would treat tumors elsewhere in a patient, the virus would have done so for reasons of inherency. With regard to Rodgers et al., the art was provided to illustrate that patients that exhibit metastases in liver also exhibit metastases in hepatic lymph nodes. Again, it is reiterated that because Kooby et al. teach the steps of the claimed method, Kooby et al.'s method would inherently treat metastases distal to the site of resection, including metastases in hepatic lymph nodes.

Applicant indicates that tumor resection and administration of virus taught by Kooby are done for a different purpose than in the present invention: prevention of local recurrence (Kooby) and the treatment of metastases (the present invention). Applicant's invention thus provides a new use. This use would not have been obvious over the teachings of Kooby and Rodgers because the references provide no teaching or suggestion of the treatment of metastases (Applicant's response, page 8). In response, Kooby et al. teach metastases. While Applicant indicates that the cancer taught by Kooby is a local recurrence, it is noted that Kooby et al. teach that the cancer is metastatic and as far as can be told, metastatic cancers seed various tissues throughout the body. As indicated above, while Kooby et al. focus on treatment of metastatic tumors in liver, this is not indicative that metastatic tumors only occur in liver. As such, because Kooby et al. teach metastases, Kooby et al. meet the limitation of the claims.

Applicant indicates that it was simply not known that virus administered to a surgical bed could travel from the site of the surgical bed by any means (including via the lymphatic system) (Applicant's response, pages 8-9). In response, as discussed in previous Office Actions and above, while the art does not specifically indicate that administration of lytic herpes virus to a resected site would treat distal metastatic cancers, Kooby et al.'s method would inherently treat metastatic tumors distal to the site of resection. Kooby et al. provide guidance to resect tumors in liver and to use G207 to treat cancer cells. An artisan would have administered G207 to the resected site in order to lyse the cancer cells which may have been missed during the surgery. While an artisan may not have recognized at the time that the method steps were treating metastatic cancer, the method steps were known at the time of filing and would have been inherent to the method.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Art Unit 1632